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Pharmacokinetics and residue behaviour of clenbuterol in calves fed with milk replacer

This thesis aims at the improvement of the data basis for a possible distinction between therapeutic and illegal use of clenbuterol. Additionally the obtained results are discussed with regards to their consequences for residue control. In its first part, this thesis deals with the pharmacokinetics of clenbuterol and the most suitable time for drawing plasma samples. Another part describes the residue characteristics of clenbuterol during and after the treatment of veal calves fed with milk replacer. The experiments conducted as part of the present thesis were supported by the European Commission.

Pharmacokinetics of clenbuterol

The pharmacokinetics of clenbuterol were examined in six veal calves which had received intravenous dosages of 1, 2 and 3 µg/kg body weight and oral dosages of 2,5, 5 and 10 µg/kg body weight in a “cross-over design”.

Following intravenous application, the distribution and elimination of clenbuterol in plasma followed a two-compartment pattern. In most cases it was distributed within the first hour with a half life of 20-35 minutes. A mean value of 1.07 l/kg/h (SD 0.75 l/kg/h) was calculated for clearance. Elimination half life for the terminal phase ranged from 2.9 to 5 hours.

The resorption, distribution and elimination of clenbuterol in plasma after oral administration could best be described by a one-compartment model. Clenbuterol was rapidly resorbed. After 15 minutes an increase was already measured. The maximum concentration was reached, on average, after 3.9 hours (SD 1,64 h). Hence the best time for drawing samples would be 3 to 5 hours after an administration of clenbuterol. Elimination half life ranged from 3.4 to 19.5 hours.

In calves fed with milk replacer clenbuterol showed a good oral bioavailability of 89% (SD 17.4%). A significant dose relation could not be established for any of the pharmacokinetic parameters determined.

Clenbuterol is largely eliminated through urine. In almost all animals maximum urine concentrations were reached after 0.5 to 2.5 hours following intravenous application, and after 2.5 to 12 hours following oral application. The maximum urine concentrations were about 65 to 240 times higher than the maximum plasma concentrations.

Residue behaviour of clenbuterol

The experiments concerning the residue behaviour of clenbuterol were performed on 68 veal calves, out of which 32 animals received orally the therapeutic dosage of 2 x 8 µg/kg body weight for 10.5 days, 24 animals the fattening dosage of 2 x 10 µg/kg body weight for 21 days, and 12 animals the double fattening dosage of 10, 15 and 20 µg/kg body weight for a total of 21 days. The animals were then slaughtered after observing different withdrawal periods. Clenbuterol could be detected in the retina/uvea during the entire duration of withdrawal periods (up to 35 days). Concentrations were 20 to 50 times higher than in liver and kidney. Already after a withdrawal period of 7 days no residue concentrations exceeding the currently discussed MRL (liver, kidney: 0.5 ng/g and muscle: 0.1 ng/g) could be detected in muscle, liver and kidney of those animals that had received the therapeutic dosage. Neither was clenbuterol detected in muscle of animals that had received the single or double fattening dosage. Hence given the currently applicable withdrawal period of 28 days, any positive result for clenbuterol in a matrix other than retina/uvea obtained by samples taken at the slaughterhouse would necessarily result from failure to comply with the required withdrawal period or from illegal use.

Additional plasma samples were taken from six animals receiving the therapeutic dosage, 5 animals receiving the fattening dosage and 3 animals receiving the double fattening dosage before, during and after treatment. The analysis results of these samples showed that the limit of 2 µg/kg suggested by Quirke (1994a) for the discrimination between therapeutically and illegally treated animals is much too high. Most of the clenbuterol concentrations in the plasma of animals treated with an illegal dosage did not exceed this limit either. An unambiguous distinction of veal calves having received a therapeutic dosage from those having received a higher dosage was impossible even when applying a lower limit. Neither were other matrices, such as faeces, urine or hair, suited to monitor the legal use of clenbuterol for therapeutic reasons in food-producing animals.

It can be concluded from these results that a therapeutic use of clenbuterol cannot be controlled effectively either on animal farms or at slaughterhouses. The far-reaching ban of clenbuterol in food-producing animals issued by the European Commission can thus be an effective way of controlling the clenbuterol abuse.